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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/468,610	06/06/1995	SIMON C. BURTON	010055-134	5415

5100 7590 11/22/2002

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EXAMINER

WEBER, JON P

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 11/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application N .

08/468,610

Applicant(s)

BURTON ET AL.

Examiner

Jon P Weber, Ph.D.

Art Unit

1651

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: New limitations not previously considered.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

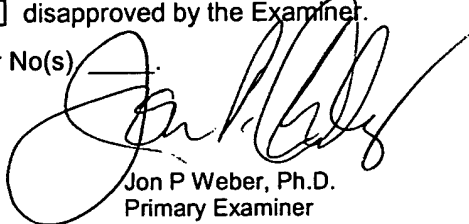
Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-5,7-23,55 and 56.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

  
Jon P Weber, Ph.D.  
Primary Examiner  
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### ***Status of the Claims***

The response with amendments filed 18 October 2002 has been received but will not entered because amendments present new limitations that have not previously been considered. Claims 1-5, 7-23, 55 and 56 have been presented for examination.

### ***Double Patenting***

Claims 1-5, 7-23 and 55-56 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 26-28 of U.S. Patent No. 5,652,348.

It is argued that the examiner in the conflicting patent did not raise a double patenting rejection even though the examiner was apprised of the parent application of the instant application, 08/268,178, in the response of 29 August 1995. It is also argued that this parent application was filed three months prior to the conflicting patent, hence the patent is not prior.

A review of the file history of the patent shows that parent application, 08/268,178, was brought to the examiner's attention in the context of prior art which had been cited in both the patent and said parent. A copy of the initialed 1449 had not been provided with the Office action of 01 May 1995 and that was desired.

There is no evidence in the record to indicate that the examiner considered 08/268,178 for double patenting. The record suggests that the examiner simply provided signed and initialed copies of the 1449 with the final rejection of 18 December 1995 without any further comment.

Assuming, *in arguendo*, that the other examiner considered making a double patenting rejection, since the '100 application was ready for allowance while the instant application was

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pending, the MPEP states that the double patenting rejection should be dropped for the first application to issue. Hence, even if it had been made it would have been dropped. In either case the result would be the same.

That being said, the question remains to the validity of a double patenting rejection. Since, the basis of the rejection was not traversed, it is presumed that the reasons for making a double patenting rejection are acquiesced, that is, the instant claims are obvious over the patent.

With respect to the date of the parent being three months older than the patent, it is noted that a Terminal Disclaimer serves two purposes: 1) to assure that there is no improper term extension, and 2) to assure that both patents **remain** commonly owned.

Accordingly a double patenting rejection is proper and is maintained.

### ***Claim Rejections - 35 USC § 112***

Claims 55-56 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is argued that new matter is not present. Support for thiol and hydroxyl groups is alleged at least at page 24, lines 5-10. It is argued that this shows that these groups are reactive groups on the ligand. It is urged that these groups are ionizable groups within the meaning of the disclosure.

It is respectfully pointed out that the citation referenced establishes that these groups are used to link the ligand to the support matrix but are not themselves pendant after linking. The

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disclosure goes on to state, "In this resin, the ligand is attached through a stable thioether bond." The subsequent examples, such as mercaptobenzimidazole, make it clear that the thiol is used to link the ionizable ligand (e.g. an imidazole moiety) to the support but is not the ionizable ligand itself.

It is agreed that hydroxyls and thiols could be ionizable ligands, but the disclosure does not provide a positive recitation of these groups as ionizable ligands.

Applicant's arguments filed 18 October 2002 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 112, first paragraph is adhered to for the reasons of record and the additional reasons above.

***Claim Rejections - 35 USC § 102***

Claims 1-2, 4-5, 10-16, 18, 20 and 22-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Boardman et al. (1953).

The same arguments as raised in the response of 27 March 2002 are reiterated. It is asserted that the Declarations show that pH 6.1 is the pKa of the IRC-50 resin, so the resin is still 50% charged at this pH. It is asserted that the Declarations show that at pH 5.0 the resin retains a partial charge of 20%, which is greater than the "less than 5%" as required by the disclosure. It is urged that the experimental titration curve is more accurate than theoretical calculations of Henderson-Hasselbach. It is argued that Boardman fails to define "almost wholly undissociated." It is also argued that the rejection appears to rely upon Topp, Kunin, and Kitchener references and that the rejection should be under 103.

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The most salient feature of Boardman, the titration curves shown in Figure 1, seems to have been overlooked. Clearly at pH 5.0, cytochrome C is bound, and elutes between pH values of 6-7 or 6-8 depending on ionic strength. Concomitantly, the resin takes up the sodium ions. Boardman also uses the resin to separate two carboxyhemoglobins with isoelectric points of 6.7 and 7.3 (Figure 2) at a pH of 5.8. The titration curve of the resin in the absence of protein may differ than with the protein. The arguments with respect to the Declarations have been discussed in the Office action of 21 June 2002 and will not be restated. It is agreed that Boardman does not define the term "almost wholly undissociated", but taking its plain meaning suggests that the resin would meet the claim limitations. The Topp, Kunin, and Kitchener references were relied upon solely for their teachings of inherent properties, explanation of what the curves are showing, and for a larger figure of the titration curve of this resin. To assert that they are relied upon in an obvious type rejection is unwarranted.

Applicant's arguments filed 18 October 2002 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 102(b) is adhered to for the reasons of record and the additional reasons above.

### ***Claim Rejections - 35 USC § 103***

Claims 1-5, 7-23 and 55-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Boardman et al. (1953), Sasaki et al. (1979) and Sasaki et al. (1982) in view of Kunin (1958), Topp et al. (1949), Kitchener (1957) and Guthrie (1957) and further in view of Hancock et al. (US 4,401,629), Kitamura et al. (JP 01211543), Tokuyama (JP 60137441), Kondo et al. (JP

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61033130), Iimuro et al. (US 4,950,807), Bruegger (US 4,810,391), Economy et al. (US 3,835,072), Jones et al. (US 4,154,676).

It is argued that the Board found that the Sasaki references do not obviate the instant claims because the references lack a resin that undergoes the transition between uncharged and charged between pH values of 5-9. It is urged that Sasaki references teach away because the resin they use suggests a pH value of 4.5 or less is necessary. It is urged that Sasaki references do not motivate substituting other resins. It is urged that Boardman teaches away too because it is only at "very low pHs" that the resin is fully charged. It is urged that the additional references teaching resins containing functional groups that may be ionizable fail to teach using these resins to purify proteins. Finally it is argued that combining fifteen references shows that the claimed invention is non-obvious.

The Board decision has been selectively interpreted. What the Board said is:

The examiner has asserted that "resins are known in the art which would be uncharged within the pH range of the scope of the claims." However, the examiner has not favored the record with any evidence in support of this assertion. As the record now stands, the prior art does not describe any resin which meets the requirements of the claims on appeal. In other words, the claimed resins are novel. If the examiner is aware of resins "known in the art which would be uncharged within the pH range of the scope of the claims," it is incumbent upon him to provide evidence in the record documenting the fact. The examiner has not done so.

It was solely on this basis that the rejection was not affirmed. The Office action of 21 June 2002 provided the series of secondary references establishing the resins meeting the claim limitations were well known in the art. Specific examples of claimed functional groups pendant on the support were provided by these references. A large number of such references were cited to establish a large number of specifically recited functional groups. Hence, the record now clearly shows that such resins are well known in the art. It is not an assertion by the examiner as

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remarked by the Board. Further, the large number of references was provided solely for completeness. It was desirable to demonstrate that a large number of suitable functional groups were known in the art to be appended to supports.

Neither the Sasaki references nor Boardman teach away from the claimed invention. Sasaki provides a general concept and all of these three references merely provide specific examples. As is well known, the examples are non-limiting to the concept. They only provide working evidence of concept, unless there is some reason to believe the examples are the only possibility. In the instant case, the explanatory cartoon in Sasaki belies that suggestion. No specific pH values are given. Boardman is simply a specific example. They did not clearly contemplate the same concept as Sasaki.

Applicant's arguments filed 18 October 2002 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 103(a) is adhered to for the reasons of record and the additional reasons above.

### ***Withdrawal of Finality***

It is again argued that the double patenting rejection is in error and that the Office had previously determined that the '100 application was not material to patentability. Hence, it is argued that concluding that applicants failure to disclose the '100 application contravenes the duty to disclose is unjust to applicants. It is argued that even if the double patenting rejection is proper and applicants were required to disclose the conflicting application, the addition of the eight new references was not required by amendment. Accordingly it is urged that the finality is premature.



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The double patenting rejection has been discussed above. Further, there was never any disclosure of the '100 application in the '178 application or this application. The failure to disclose this possible double patenting situation is applicants'.

The newly added references were made in response to newly added claims 55-56 which recite specific ionizable ligands that had not previously been presented. To address these new limitations, it was necessary to demonstrate that resins having these specific functional groups appended were known in the art. Hence, the rejection was necessitated by amendment.

Thus, the argument that the final rejection is premature is not persuasive. The finality will not be withdrawn and the period for response continues to run from the date of mailing of the final Office action, instantly extended to four months.